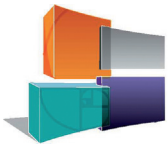
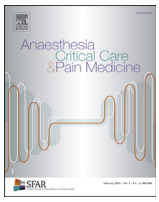
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Anaesth Crit Care Pain Med xxx (2020) xxx–xxx



SFAR
Société Française d'Anesthésie et de Réanimation



Letter to the Editor

Low total cholesterol blood level is correlated with pulmonary severity in COVID-19 critical ill patients

Dear Editor,

Lipid disturbances have recently been highlighted as a possible pathway in COVID-19 pathogenicity [1]. Indeed, a decrease in serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) and different apolipoproteins is associated with poor prognosis in patients with COVID-19, and may be an important feature to consider in understanding the pathophysiology of COVID-19.

To explore this pathway, we conducted a retrospective single centre study on prospectively collected data. Every patient admitted in Saint-Louis Hospital's Surgical Intensive Care Unit (ICU) (Assistance Publique - Hôpitaux de Paris, Paris, France) for respiratory failure related to COVID-19 and who had an exploration of lipid abnormalities at ICU admission was included. Exclusion criteria were age under 18, pregnancy or moribund patient at admission.

Methods to determine cholesterol blood levels (TC, LDL-c, HDL-c, triglycerides) were enzymatic colorimetry and immunoturbidimetry for apolipoproteins (A1 and B).

All patients or their surrogate had information about the data collection and gave their non-opposition to the study (Ethical committee of the French Society of Anaesthesia and Intensive Care [SFAR] IRB 00010254 - 2019 – 203). Continuous variables were described as median with their interquartile ratio (IQR) while categorical variables were expressed as frequencies (%). After a normality test, data were analysed with a Mann-Whitney or a Student *t*-test according to their distribution with a 5% first species risk. Spearman correlation test was used.

Of 54 COVID-19 patients admitted in our ICU from March 20, 2020 to April 15, 2020, thirty-one patients had an exploration of lipid abnormalities at admission (LDL-c, HDL-c, TC, apolipoproteins A1 and B (ApoA1 and B)). Patients' characteristics are summarised in Table 1, and biological results of lipid profile in Table 2. Among the 31 patients included, dyslipidaemia was not associated with mortality (Table 1). Pre-admission lipid lowering drugs prescription was associated with lower LDL-c, TC and Apo on admission (0.72 *vs* 1.33 mmol/L; $p = 0.043$, 2.46 *vs* 2.95 mmol/L; $p = 0.049$ and 0.55 *vs* 0.74 mmol/L; $p = 0.037$, respectively) and a trend for a higher in-hospital mortality (42.9% *vs* 12.5%, $p = 0.110$). Only 27 patients had a lipid exploration and PaO_2/FiO_2 data available. In these patients, we observed a correlation between PaO_2/FiO_2 at admission and TC and HDL-c (Fig. 1A and C; $r = 0.642$, $p < 0.001$

Table 1
Characteristics of patients.

	All patients (n = 31)	Survivors (n = 24)	Non-survivors (n = 7)	*p*
Age (y)	63 [60–68]	62 [60–67]	74 [64–76]	0.039
Weight (kg)	83 [71–88]	83 [72–92]	83 [77–86]	0.232
Size (cm)	172 [162–176]	173 [165–176]	167 [159–174]	0.858
BMI (kg/m^2)	27 [26–30]	27 [26–30]	27 [26–33]	0.646
Sex male, n (%)	24 (77.4)	19 (79.2)	5 (71.4)	0.642
Comorbidities				
Tobacco use, n (%)	2 (6.5)	2 (8.3)	0 (0.0)	1
Hypertension, n (%)	17 (54.8)	12 (50.0)	5 (71.4)	0.412
ACEi or ARBS, n (%)	9 (29.0)	7 (29.2)	2 (28.6)	1
Diabetes mellitus, n (%)	10 (32.3)	6 (25.0)	4 (57.1)	0.172
Dyslipidaemia, n (%)	8 (25.8)	4 (16.7)	4 (57.1)	0.053
Coronary disease, n (%)	1 (3.2)	1 (4.2)	0 (0.0)	1
Chronic pulmonary disease, n (%)	4 (12.9)	3 (12.5)	1 (14.3)	1
Severity of illness				
Radiological lesions > 50%, n (%)	19 (61.3)	13 (54.2)	6 (85.7)	0.201
SAPS II	37 [29–44]	37 [31–44]	37 [29–42]	0.920
SOFA	4 [4–7]	5 [4–7]	4 [4–7]	0.820
Organ failure during ICU stay				
ARDS, n (%)	26 (83.9)	20 (83.3)	6 (85.7)	1
Admission PaO_2/FiO_2 (mmHg)	127 [80–176]	143 [82–183]	88 [80–104]	0.122
Worst PaO_2/FiO_2 (mmHg)	81 [72–109]	86 [75–138]	72 [71–79]	0.062
AKI, n (%)	16 (51.6)	10 (41.7)	6 (85.7)	0.083
RRT, n (%)	4 (12.9)	1 (4.2)	3 (42.9)	0.028
Norepinephrine in first 48 h, n (%)	14 (45.2)	10 (41.7)	4 (57.1)	0.671

ACEi: angiotensin converting enzyme inhibitor; AKI: acute kidney injury; ARBS: angiotensin receptor blockers; ARDS: acute respiratory distress syndrome; BMI: body mass index; ICU: intensive care unit; SAPS II: simplified acute physiology score II; SOFA: simplified organ failure assessment, RRT: renal replacement therapy.

https://doi.org/10.1016/j.accpm.2020.07.015

Table 2
Lipid profile for COVID-19 patients.

	All patients (n = 31)	Survivors (n = 24)	Non-survivors (n = 7)	*p*
LDL-c (mmol/L)	1.40 [1.22–2.20]	1.63 [1.37–2.52]	0.82 [0.53–1.37]	0.004
HDL-c (mmol/L)	0.72 [0.61–0.93]	0.85 [0.47–1.30]	0.67 [0.62–1.10]	0.285
Total cholesterol (mmol/L)	2.89 [2.56–3.57]	3.12 [2.78–4.11]	2.38 [1.95–2.75]	0.007
Triglycerides (mmol/L)	1.43 [1.10–1.86]	1.43 [1.03–1.87]	1.48 [0.81–1.62]	0.563
Apolipoprotein A1 (mmol/L)	0.69 [0.56–0.80]	0.74 [0.55–0.88]	0.59 [0.57–0.85]	0.567
Apolipoprotein B (mmol/L)	0.71 [0.61–0.89]	0.79 [0.67–0.95]	0.60 [0.46–0.69]	0.008

HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol.

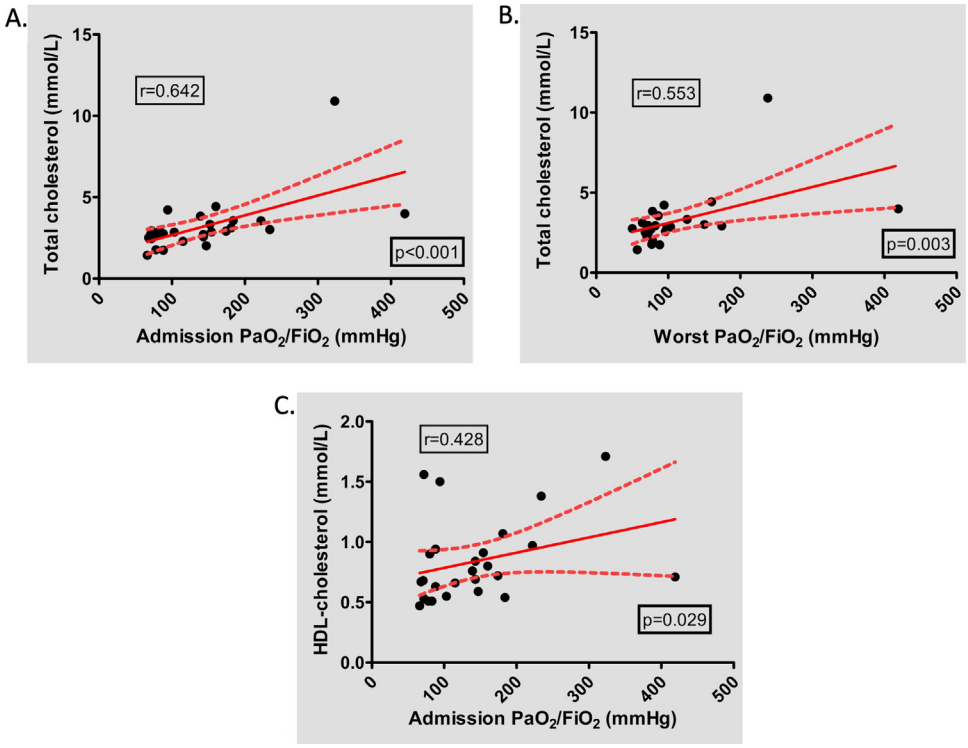


Fig. 1. Correlation between lipid abnormalities at ICU admission and PaO_2/FiO_2 during ICU stay.
HDL: high-density lipoprotein.

and $r = 0.428$, $p = 0.029$, respectively) and between worst PaO_2/FiO_2 and TC (Fig. 1B; $r = 0.553$, $p = 0.003$). Furthermore, in bivariate analysis including age and LDL-c level, LDL-c level was associated with 28-day mortality, whereas age was not (OR = 0.0233 [CI 95% 0.0006–0.8835], $p = 0.0427$ *vs* OR = 1.0291 [CI 95% 0.8794–1.2044], $p = 0.7203$, respectively).

Our results suggest a role of lipid disorders in COVID-19 severity as proposed by Cao and colleagues [1]. The decrease in TC could result from vasculopathy induced by SARS-CoV-2. Indeed, we observed a correlation between TC blood level and COVID-19 severity, assessed by PaO_2/FiO_2 ratio. Our series suggests that COVID-19 severity is linked with lipid level. It might be interesting to practice lipid dosage in broncho-alveolar lavage to assess if there is an intra alveolar lipid extravasation, alveolar obstruction and inflammation. Whether lipid-lowering treatments (*i.e.,* statins) could be associated with COVID-19 severity remains to be explored in larger studies. Experimental data suggest that statins have potential benefits in acute respiratory distress syndrome (ARDS), including anti-inflammatory properties, immunomodulatory, antioxidant, and antithrombotic effects. Nevertheless, clinical trials failed to show a benefit of statins administration in patients with ARDS [2]. A possible explanation of failure of statins therapy in patients with ARDS could be partly explained by an increase in interleukin-18 level induced by statin therapy [3]. In COVID-19, interleukin-18 is associated with severity of the disease [4] and is also believed to be a potential therapeutic target [5]. More explorations are required to better understand and explain the role of lipid pathways in COVID-19 pathophysiology.

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

None.

Authors' contribution

QR, ED and FD designed the study, collected the data and drafted the manuscript.

NM conducted the assays and drafted the manuscript.

MC drafted the manuscript.

All authors approved the final version of the manuscript.

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